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Cell-mediated immunotherapy of cancer by intentionally mismatched donor lymphocytes

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Chemotherapy-resistant hematopoietic malignancies and metastatic solid tumors remain incurable due to residual multi-drug resistant cancer cells after conventional anti-cancer modalities and cancer stem cells that are a priori resistant to available anti-cancer modalities. We have previously documented that patients with hematological malignancies fully resistant to myeloablative chemoradiotherapy may be cured by donor lymphocyte infusion [DLI] following failure of myeloablative stem cell transplantation (SCT), indicating that alloreactive lymphocytes can eliminate "the last cancer cell" regardless of resistance to all available anti-cancer modalities. When immunotherapy by donor lymphocytes is applied following allogeneic SCT, elimination of resistant cancer cells may be accomplished at the cost of hazardous, not infrequently fatal, acute and chronic graft-vs-host disease [GVHD]. We have developed a new approach for elimination of resistant malignant cells using safe outpatient procedure based on the use of intentionally mismatched, related haploidentical or even unrelated donor lymphocytes, activated in vitro and in vivo with low dose interleukin 2 [IL-2] including activated T & NK cells. No GVHD develops because intentionally mismatched killer cells are always rejected after less than 7-10 days, before there is any chance for GVHD to develop. IL-2 activated intentionally mismatched donor lymphocytes, including T cells and NK cells, can induce very potent anti-cancer effects without causing GVHD. Anti-cancer effects of intentionally mismatched donor lymphocytes can be further amplified by targeting killer cells against residual malignant cells using monoclonal and bispecific antibodies against antigens over-expressed on targeted malignant cells. In conclusion, accordingly, based on our successful cumulative pre-clinical experimental data and ongoing clinical experience, clinical application of intentionally mismatched killer cells at the stage of minimal residual disease may represent a simple, safe and cost-effective procedure that my result in cure in patients with otherwise incurable cancer.

Speaker Biography

Shimon Slavin is the professor of medicine and he is also the medical and scientific director at the Biotherapy International.

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